AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Previously presented) A method of identifying a RAS-related C3 botulinum toxin substrate (RAC) pathway modulating agent, said method comprising the steps of:

(a) providing an assay system comprising a Maternal Embryonic Leucine Zipper Kinase (MELK) polypeptide comprising SEQ ID NO: 6 or nucleic acid encoding SEQ ID NO: 6, wherein the assay system is capable of detecting the activity or expression of MELK;

(b) contacting the assay system with a test agent that modulates the activity or expression of MELK; and

(c) determining the activity or expression of the MELK polypeptide or nucleic acid in the assay system in the presence or absence of the test agent of step (b), wherein a change in MELK activity or expression between the presence and absence of the test agent identifies the test agent as a candidate RAC pathway modulating agent;

(d) providing a second assay system comprising cultured cells or a non-human animal expressing MELK capable of detecting a change in the RAC pathway,

(e) contacting the second assay system with the test agent of step (b); and

(f) measuring the RAC pathway in the presence or absence of the test agent, wherein the detection of a difference in the presence and absence of the test agent confirms the test agent as a RAC pathway modulating agent.

2. (Previously presented) The method of Claim 1 wherein the first assay system comprises cultured cells that express the MELK polypeptide.

3. (Original) The method of Claim 2 wherein the cultured cells additionally have defective RAC function.

4. (Previously presented) The method of Claim 1 wherein the first assay system includes a screening assay comprising a MELK polypeptide, and the candidate test agent is a small molecule modulator.

5. (Previously presented) The method of Claim 4 wherein the screening assay is a kinase assay.

6. (Previously presented) The method of Claim 1 wherein the second assay system is selected from the group consisting of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. (Previously presented) The method of Claim 1 wherein the first assay system includes a binding assay comprising a MELK polypeptide and the candidate test agent is an antibody.

8. (Previously presented) The method of Claim 1 wherein the first assay system includes an expression assay comprising a MELK nucleic acid and the candidate test agent is a nucleic acid modulator.

9. (Original) The method of claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. (Previously presented) The method of Claim 8 wherein the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO).

11. (Currently amended) The method of Claim 1 ~~additionally comprising:~~
wherein the second assay system comprises cells defective in RAC function and is capable of detecting a phenotypic change in the model system that indicates that the RAC function is restored when compared relative to wild-type cells.

12. (Original) The method of Claim 11 wherein the model system is a mouse model

with defective RAC function.

13. -25. (Canceled)